

Application No. 10/008,575
Amendment dated September 11, 2003
Response to Office Action of March 11, 2003

Please replace the paragraph beginning at page 1, line 2, with the following rewritten paragraph:

A1
This application is ~~a continuation in part~~ claims benefit of United States Provisional Application No. 60/246,450, filed November 7, 2000.

Replace the paragraph beginning at page 2, line 21, with the following rewritten paragraph:

A2
Animal models for muscle protein wasting can be treated with inhibitors of muscle protein wasting (caspase 3 inhibitors). Suitable animal models include, but are not limited to, rats in which diabetes has been induced by streptozotocin. The present invention further provides a method for increasing muscle mass or preventing loss of muscle mass in a subject achieved by administering to the subject an effective amount of a caspase enzyme inhibitor or an inhibitor of an activator of caspase enzyme ~~ord~~ or of the enzymes that activate caspases (e.g., enzymes or chemicals that block the activity of phosphatidylinositol 3-kinase). Muscle mass is increased in a normal human or animal, in a human or animal recovering from a muscle wasting condition or in a patient with a catabolic condition. Alternatively, inhibitors of specific caspase enzymes (e.g. caspase 3) or inhibitors of the activation of caspase enzymes (e.g., a dominant negative gene or myoblasts transfected to express an inhibitor of caspases) can be introduced locally into muscle. Likewise, a "muscle-specific" gene could be used to avoid a generalized suppression of apoptosis events in other tissues/organs in animals and in the future, patients. A reduction in the amount of the actin degradation product in a muscle biopsy sample is characteristic of a positive response to the treatment. Similar studies can be carried out with muscle cells in culture, with actin proteins and degradation products being resolved using size separation techniques and identified with an actin-specific antibody.

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Replace the paragraph beginning on page 10, line 8, with the following rewritten paragraph:

03
Antibodies specific for Arg-gingipains actin or cross-reactive protein of 14-15 kDa may be useful, for example, as probes for screening DNA expression libraries or for detecting the presence of Arg-gingipains actin or cross-reactive protein of 14-15 kDa in a test sample. Frequently, the polypeptides and antibodies will be labeled by joining, either covalently or noncovalently, a substance which provides a detectable signal. Suitable labels include but are not limited to radionuclides, enzymes (including but not limited to, alkaline phosphatase and horse radish peroxidase), substrates, cofactors, inhibitors, fluorescent agents, chemiluminescent agents, magnetic particles and the like. United States Patents describing the use of such labels include but are not limited to Nos. 3,817,837; 3,850,752; 3,939,350; 3,996,345; 4,277,437; 4,275,149; and 4,366,241.

Replace the paragraph numbered 18 on page 14, with the following rewritten paragraph:

- 24
18. Isozaki, Y. et al. Interaction between glucocorticoids and acidification results in stimulation of proteolysis and mRNAs of proteins encoding the ubiquitin-proteasome pathway in BC3H-1 myocytes. Protein degradation and increased mRNAs encoding proteins of the ubiquitin-proteasome proteolytic pathway in BC3H1 myocytes require an interaction between glucocorticoids and acidification. *Proc. Natl. Acad. Sci. USA* 93, 1967-1971 (1996).